IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of	: Stefan HENKE, et al	) Art Unit:	16511
U.S. Appln. No.	: 10/694,569	) Examiner:	Kyle A. PURDY
Confirmation No.	: 3543		
U.S. Filing Date	: October 27, 2003		
Title of Invention	: WATER-SOLUBLE MELOXICAM GRANULES		
Atty. Docket No.	: 01-1405		

VIA EFS Web
Commissioner for Patents
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132

Sir:

I, Dr. Martin Folger, being duly warned, declare that:

1. I am a citizen of Germany, residing in Ingelheim, Germany. I am an inventor of the above-identified patent application and am, therefore, familiar with the invention described in this application.

2. If a patent issues from this application and if it is decided by the assignee to pursue a commercial product falling under its claims, I and the other inventors may receive some income derived from such sales.

3. I received a Dr. rer. nat. degree (doctor of natural sciences) from the Technical University of Braunschweig, Germany, in 1994 after having been a graduate student at the Institutes for Pharmaceutical Technology at the Philipps University of Marburg, Germany, from 1990 to 1991 and at the Technical University of Braunschweig from 1991 to 1994. I studied Pharmaceutics at the University of Münster, Germany from 1983 to 1987 and received the approbation as a pharmacist in 1988.

4. I presently hold since 2002 the position of Head of Pharmaceutical Development at Boehringer Ingelheim Vetmedica GmbH, Ingelheim, Germany, where my research focuses on formulation development, process development, and analytical development of veterinary pharmaceutical products. Prior to this appointment I held from 1997 to 2002 the position of lab manager where my researched focused on formulation development of veterinary pharmaceutical products.

5. I am a named author on 5 literature publications in the fields of pharmaceutical technology. I am a named inventor on 9 patents and published patent applications in the fields of application of formulations and their respective processes for manufacturing. I consider myself one of ordinary skill in the art in the field of pharmaceutical research and development.

6. As noted above, I am familiar with the subject application and understand that the amended claims in their broadest embodiment cover water soluble meloxicam granules comprising: (a) meloxicam, (b) a salt forming agent which forms the meglumine, sodium, potassium, or ammonium salt of meloxicam, (c) a binder; (d) a sugar or sweetener, and (e) a carrier.

7. I have read the final Office Action mailed on December 11, 2008 ("the final Office Action") in which the Examiner rejected pending claims 1-19 and 21-25 as being obvious over U.S. Patent No. 6,869,948 to Bock et al. ("Bock") in view of U.S. Publication No. 2004/0204413 to Faour et al. ("Faour").

8. In the Office Action in Section 8, page 3, the Examiner states that

> Bock is directed to oral meloxicam compositions. A granule formulation is disclosed in Example 7. The meloxicam granules comprise meloxicam, sodium citrate, lactose (carrier) (see instant claims 1 and 13-16), polvinylpyrrolidine (povidone; a binder) (see instant claims 1, 3 and 4). It is taught that the meloxicam may be a sodium or meglumine salt (see claim 1; see instant claims 1 and 2). The ratio between the meglumine and meloxicam is taught to be from 1.2:1 to 1:1.2 (see instant claims 18 and 19). The concentration of meloxicam in the granules is about 3.5% by weight (see Example 7; see instant claim 17).

9. In the Office Action in Section 9, page 4, the Examiner further states that "Bock fails to teach 5 g of their meloxicam granules as being capable of dissolving in 100 mL of demineralised water within 1 minute."

10. In the Office Action in Section 10, page 4, the Examiner states that "Faour is directed to [a] pharmaceutical composition containing a COX-II inhibitor and a muscle relaxant which may be in the form of a granule. An exemplified COX-II inhibitor is meloxicam (see claim 1)."

11. The Examiner states in Section 10, page 4 of the Office Action that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Bock and Faour with a reasonable expectation of success in arriving at a water soluble granular composition comprising meloxicam melamine, a binder, a sweetener, a carrier and an optional flavorant."

12. The Examiner further states in Section 10, page 4 of the Office Action that

> Bock and the instant composition are essentially identical except for lacking of the sweetener and optional flavorant, otherwise the compositions are identical. It is acknowledged that Bock does not teach 5 grams of their granules as possessing the ability to dissolve in 100 mL of water. However, because the compositions are essentially identical, except for the sweetener, one would expect both to have similar pharmacological and physical properties.

13. The Examiner states in Section 10, page 4 that "absent any secondary evidence, ... the granules of Bock possess similar dissolution properties as that instantly claimed."

14. I refer to Figure 4 and Example 7 in Bock which describe meloxicam meglumine salt tablets or meloxicam (granulated) capsules and the resultant drug plasma levels in patients who orally ingested these formulations. I note the data depicted in Figure 4 refers to the plasma concentration, which is indicative of the amount of dissolved meloxicam. However, the plasma concentration data depicted in Figure 4 provides no indication that the all of the components of the granule dissolved, including excipients.

15. I further note that the granulated capsule composition described by Bock in Example 7 contains cross-linked polyvinylpyrrolidone, silicon dioxide and microcrystalline cellulose. Each of these ingredients is insoluble in water including water based compositions encountered *in vivo*. I also note that including a sweetener or sugar into the granulated composition of Bock would have little effect on the solubility of the cross-linked polyvinylpyrrolidone, silicon dioxide and microcrystalline cellulose. Thus, the meloxicam (granulated) composition described by Bock in Example 7 would not be expected to be completely water soluble, even if combined with a sugar or sweetener as described in Faour. I also note that nothing in Faour suggests that the water-insoluble components used in Bock's granulated capsules should be replaced with water-soluble components.

16. I understand that independent claim 20 relates to water soluble meloxicam granules comprising meloxicam, meglumine, hydroxypropylmethylcellulose, povidone, and glucose monohydrate. I also understand that the Examiner rejected claim 20 of the subject application as being obvious over Bock in view Faour and D. M. Parik, Handbook of Pharmaceutical Granulation Technology, 1st edition, pp. 60-72, 1997 ("Parikh").

17. In the office action in Section 16, page 9 the Examiner states that

> Parikh is drawn to a variety of binders to be used in granulating granules. It is taught that binders are provided to provide a cohesive force to the granules. Binders include natural and synthetic binders such as povidone and hydroxypropyl methylcellulose (HPMC).

18. In the office action in Section 16, page 6 the Examiner further states that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Bock, Faour, and Parikh with a reasonable expectation of success in arriving at a water soluble granule composition comprising meloxicam, meglumine, HPMC, povidone and glucose monohydrate."

19. As I discussed above in Paragraphs 14 and 15 the granulated capsule composition described by Bock in Example 7 and depicted in Figure 4 contains components that are not water soluble, i.e., cross-linked polyvinylpyrrolidone, silicon dioxide and microcrystalline cellulose. Nothing in Parikh suggests that these water-insoluble components should be replaced by water-soluble components. Thus, even if the granulated capsule of Bock was modified to include povidone and HPMC, nothing in Parikh suggests replacing the other water-insoluble components used in Bock's granules, i.e., silicon dioxide and microcrystalline cellulose.

20. In summary, the granulated capsule described in Example 7 and Figure 4 of Bock contains water-insoluble components (cross-linked polyvinylpyrrolidone, silicon dioxide and microcrystalline cellulose), so the granulated capsule of Bock will not completely dissolve in water. Nothing in Faour or Parikh would lead me to modify the granulated composition of Bock to replace these water-insoluble components with water-soluble components.

21. All statements made herein are of my own knowledge, are true and all statements made on information and belief are believed to be true. All statements made herein are made with the knowledge that false statements and the like so made are punishable by fine

or imprisonment or both, under Section 1001 of Title 18 of the United States Code, in that willful false statements may jeopardize the validity of the above-identified application or any patent that may issue from it.

Date: May 5, 2009

Dr. Martin Folger